UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/909,379	07/06/92	SCHMITT-WILLICH	H SCH-1199

EXAMINER
CHAPMAN, L

22M2/0706
MILLEN, WHITE, ZELANO & BRANIGAN, P. C.
ARLINGTON COURTHOUSE PLAZA 1, STE. 1400
2200 CLARENDON BLVD.
ARLINGTON, VA 22201

ART UNIT	PAPER NUMBER
2203	17

DATE MAILED: 07/06/94

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☐ This application has been examined ☑ Responsive to communication filed on 3/30/94 & 4/22/94 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 1-35 are pending in the application.
   Of the above, claims 11-16, 33-35 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 1-10, 17-32 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 2/93)

1. Applicant's amendments filed 3/30/94 and 4/22/94 have been entered. New claims 33-35 are drawn to a non-elected species, namely to a DTPA derivative without a benzoxy side chain. Thus, these claims are withdrawn from conderation as being drawn to a non-elected invention. Applicant's arguments filed 3/30/94 have been carefully considered and have been found partially persuasive.

2. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

3. Claims 1-10 and 17-32 are rejected under 35 U.S.C. § 103 as being unpatentable over Berg et al. in view of Gries et al.

Berg et al. disclose DTPA derivatives "particularly useful for the preparations of diagnostic and therapeutic agents for magnetic resonance imaging, scintigraphy, ultrasound imaging, radiotherapy and heavy metal detoxification" (Abstract). The compounds of the Berg et al. invention contain pendant groups designated R1 which correspond to Applicant's Z substituents. Applicant's attention is drawn to the compounds listed in columns 14-16 and particularly to the structure IK in column 16. Berg et al. teach in the Abstract that R1 may be a hydrogen atom, a hydroxyalkyl group, or an optionally hydroxylated alkoxy or alkyloxy group. In column 3, line 39-50, Berg et al. discuss the metal ions to which the chelate can

complex: "It is...particularly preferred that the number of the ion-forming groups X in the compounds of formula I be chosen to equal the valency of the metal species to be chelated by the compound of formula I. Thus, for example, where Gd(III) is to be chelated, the chelating agent of formula I preferably contains three ion-forming X groups...." Although Berg et al. disclose pendant alkyloxy substituents, they do not mention benzoxy substituents such that a benzyl group would be substituted for the alkyl portion of the pendant alkyloxy group.

Gries et al. disclose DTPA derivatives with pendant R1 groups which correspond to Applicant's Z substituents. Applicant's attention is directed to Formula I and the Abstract. Gries et al. teach in the Abstract the equivalence of alkyl groups, phenyl groups, and benzyl groups for the R1 substituent. Possible metals to which the ligands can complex are discussed on page 2 and include metals with atomic numbers of 21-29, 31, 32, 38, 39, 42-44, 49, and 57-83 which are useful for diagnostic purposes. Thus, since Gries et al. and Berg et al. both teach DTPA derivatives which complex with Gd and which are used for diagnosis, it would have been obvious to a person of ordinary skill in the art to utilize the teaching of Gries et al. to modify the invention of Berg et al. with an equivalent hydrocarbon group for the alkyl portion of the pendant alkyloxy group.

4. Applicant's arguments filed 3/30/94 with respect to the Gansow reference have been found persuasive. This reference has been dropped as a basis for rejection.

Applicant's arguments with respect to the rejection over Berg et al. in view of Gries et al. are not found persuasive. Applicant argues that Berg et al. do not teach alkyl substituents, but it is believed that applicant took the examiner's comments out of context of the rest of the rejection. In referring to "alkyl" groups and substituents, the examiner intends the alkyl portion of the alkyloxy substituents. The examiner apologizes for any confusion with the wording of the rejection, but points out that the previous rejection did state "...it would have been obvious to a person of ordinary skill in the art to modify the invention of Berg et al. by substituting a benzyl group for an alkyl group *in the ligand's side chain*" [emphasis added]. Furthermore, the rejection does not assert that the side chains of Gries et al. be substituted

for the side chains of Berg et al., but rather the side chains of Berg et al. be modified such that a benzyl group be substituted for the alkyl portion of the pendant alkyloxy group. The motivation for this substitution is the equivalence teaching of Gries et al.

Furthermore, case precedent has held the equivalence of benzyl and alkyl groups: "Cyclo-lower-alkyl and phenyl radicals are so extremely common that we believe any chemist of ordinary competence would readily realize that said radicals might be substituted for...alkyl radicals" (Ex parte Koster, 136 USPQ 75). Thus, benzoxy and alkyloxy groups are believed to be equivalent structures to the ordinarily skilled organic chemist, and substituting one for the other would have been readily obvious to this artisan at the time of applicant's invention.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lara Chapman whose telephone number is (703) 308-0450.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0511.

lc
July 1, 1994

Richard D. Lovering
RICHARD D. LOVERING
EXAMINER
GROUP ART UNIT 223